

Nabil Hanna-U.S. Patent Appl. No. 09/986,174

# I. AMENDMENT TO THE SPECIFICATION

Please delete the paragraph at page 1, line 2, and replace with the following paragraph:

-- This is the U.S. National Stage International Patent Application No. PCT/US01/40835 filed June 4, 2001, which itself claims priority to U.S. Provisional Patent Application No. 60/213,252, filed June 6, 2000. --

Please replace the paragraph [0005], with the following paragraph:

-- [0005] **Anti-CD19 Antibodies.** Antibodies have been raised which recognize CD19, a signal transduction molecule restricted to the B-cell lineage. Examples of monoclonal anti-CD19 antibodies include anti-B4 (Goullet *et al.*, *Blood* 90: 2364-75 (1997)), B43 and B43 single-chain Fv (FVS191; Li *et al.*, *Cancer Immunol. Immunother.* 47:121-130 (1998)). Myers *et al.* (*Leuk. Lymphoma* 29: 329-38 (1998)) reported conjugating the murine monoclonal B43 to the tyrosine kinase inhibitor (see also U.S. Patent No. 5,872,459 5,587,459), genistein, to produce an immunoconjugate against CD19 antigen positive hematologic malignancies. Treon *et al.*, *Semin. Oncol.* 26/5 Supp: 97-106 (1999) reported conjugation of B4 to a blocked ricin, which had no significant activity in patients with multiple myeloma. --

Please replace the paragraph [0006], with the following paragraph:

-- [0006] **Rituximab and Other Anti-CD20 Antibodies.** The FDA approved anti-CD20 antibody, Rituximab rituximab (IDEC C2B8; RITUXAN®; ATCC No. HB 11388) has also been used to treat humans. Ibritumomab (also known as ZEVALIN®) is the murine counterpart to ~~Rituximab~~ rituximab (Wiseman *et al.*, *Clin. Cancer Res.* 5: 3281s-6s (1999)). Other reported anti-CD20 antibodies include the anti-human CD20 mAb 1F5 (Shan *et al.*, *J. Immunol* 162: 6589-95 (1999); ATCC No. HB-9645), the single chain Fv anti-CD20 mouse mAb 1H4 (Haisma *et al.*, *Blood* 92: 184-90 (1998)) and anti-B1 antibody (also known as BEXXAR®) (Liu *et al.*, *J. Clin. Oncol.* 16: 3270-8 (1998)). In the instance of 1H4, a fusion protein was created reportedly fusing 1H4 with the human .beta.-glucuronidase for activation of the prodrug N-[4-doxorubicin-N-carbonyl-(oxymethyl)phenyl] O-β-glucuronyl carbamate to doxorubicin at the tumor site (Haisma *et al.* 1998). --

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*Please replace the paragraph [0080], with the following paragraph:*

-- [0080] The nucleic acid encoding an IFN- $\alpha$  (e.g., IFN- $\alpha$ -2a, IFN- $\alpha$ -2b, or IFN- $\alpha$ -n1) is operably linked to the nucleic acid encoding Rituximab such that when translated the IFN- $\alpha$  would form the carboxy terminus of the fusion protein. The antigen-binding Fc receptor-binding, C1q binding and complement (C') activation, as well as the ability of IFN- $\alpha$  to bind the NK cells and macrophages are characteristics possessed by the agents. In addition to the nucleic acid encoding ~~Rituximab~~ rituximab, other nucleic acids encoding anti-CD20 antibodies can be operably attached to the nucleic acid encoding IFN- $\alpha$ . The other anti-CD20 antibodies include ~~Idelimumab~~ ibritumomab (ZEVALIN<sup>®</sup>), IF5 (ATCC No. HB-9645), B1 (BEXXAR<sup>®</sup>) and 1H4. --